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Burden on caregivers as perceived by hemodialysis patients in the Frequent Hemodialysis Network (FHN) trials

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Abstract

Background. Patients with end-stage renal disease often rely on unpaid caregivers to assist them with their daily living and medical needs. We characterized the degree to which patients enrolled in the Frequent Hemodialysis Network (FHN) trials perceived burden on their unpaid caregivers.

Methods. Participants completed the Cousineau Perceived Burden Scale, a 10-question scale previously developed in hemodialysis (HD) patients. Associations between baseline burden score and prespecified variables were evaluated using multivariable linear regression.

Results. Of 412 participants, 236 (57%) reported having unpaid caregivers. Compared to those without unpaid care-

givers, these participants had greater comorbidity (Charlson mean 1.8 ± 1.8 versus 1.2 ± 1.7 , $P < 0.001$), lower Short Form-36 (SF-36) Physical Health Composite (PHC) scores (median 33 versus 41, $P < 0.001$, higher Beck Depression scores (mean 16 ± 11 versus 12 ± 9 , $P < 0.001$), and worse physical function. Median Cousineau score was 35 (interquartile range 20–53) (theoretical range 0–100). Over 50% felt their caregivers were overextended, yet 60% were confident that their caregivers could handle the demands of caring for them. Higher perceived burden was not associated with ability to be randomized. In adjusted analyses, Cousineau score was inversely associated with SF-36 PHC and Mental Health Composite scores and directly associated with Beck Depression score (each $P < 0.001$).

Conclusions. Most HD patients in the FHN trials perceived substantial burden on their unpaid caregivers, and self-perceived burden was associated with worse depression and quality of life. Evaluation of the effects of frequent HD on perceived burden borne by caregivers in the FHN trials will help to establish the net benefits/determents of these intensive dialytic strategies.

Keywords: burden; caregiver; depression; frequent hemodialysis; quality of life

Introduction

Patients with end-stage renal disease often rely on unpaid caregivers to assist them with their daily living and medical needs. Duties taken on by unpaid caregivers may include administration of medications, driving to dialysis and other medical appointments, maintenance of personal hygiene, provision of meals, etc. Unlike paid caregivers, unpaid caregivers are typically friends or family members, who also provide day-to-day emotional and psychosocial support. To date, relatively few studies have examined the physical, emotional and financial burden on unpaid caregivers of patients receiving dialysis [1–14]; even fewer have addressed the burden perceived by patients themselves. The latter is important as high perceptions of burden on others may be one factor contributing to poor quality of life and depression in patients receiving dialysis.

There is a growing literature on the potential benefits of home-based peritoneal dialysis and hemodialysis (HD) on health, functional capacity and independence [15], and some have suggested that more frequent HD may improve some domains of self-reported health-related quality of life (HRQoL) [16]. However, one of the potential risks of home-based and intensive dialysis therapies is that they could potentially heighten the burden shouldered by caregivers and the perceived burden of patients themselves. Thus, evaluation of the net benefits of novel dialytic therapies should include an assessment of their effects on the caregiver and the patient–caregiver relationship.

In this study, we sought to characterize the degree of burden on unpaid caregivers as perceived by patients enrolled in the Frequent Hemodialysis Network (FHN) trials at baseline [17]. We hypothesized that more extensive perceived burden would be associated with poorer self-

reported HRQoL and mental health, higher rates of depression, inability to be randomized in the trial, longer travel times to HD and greater comorbidity.

Materials and methods

Design and study population

We conducted a cross-sectional survey of patients enrolled in the FHN trials. The detailed methods of these trials have been published elsewhere [17]. Briefly, patients on conventional, thrice weekly HD for >3 months from 20 centers were invited to participate in one of the two randomized clinical trials evaluating the efficacy and safety of two frequent HD regimens [incenter ‘daily’ (six times weekly) HD compared with incenter conventional three times weekly HD or home nocturnal HD compared with home conventional three times weekly HD]. The FHN trials were approved by each center’s local institutional review or ethics board. All participants enrolled in the FHN trials were included in this cross-sectional study, irrespective of whether they finally underwent randomization or not.

Questionnaires and other data collection

During the baseline enrollment period, data were collected on subject demographics, comorbidities, laboratory variables and dialysis prescription. Participants also completed several questionnaires that were centrally administered by telephone, including the Cousineau Scale of Perceived Burden. The Cousineau scale is a 10-item questionnaire originally developed in patients on HD [18]. It assesses the degree to which patients perceive themselves as a burden on unpaid caregivers. Questions are answered on a 5-point Likert scale then summed and normalized to create an overall score ranging from 0 (no burden) to 100 (maximum burden).

Participants also completed the Medical Outcomes Study Short Form-36 (SF-36), Beck Depression Inventory (BDI) and tests of physical performance and cognitive function, as previously described [17]. The former two were centrally administered by telephone, while the latter were assessed by research staff in-person at the participants’ dialysis facilities. The SF-36 is a 36-item questionnaire assessing HRQoL with scores ranging from 0 (poorest HRQoL) to 100 (best HRQoL) and has been previously validated in dialysis patients. Self-reported physical and mental health were summarized with the RAND Physical Health Composite (PHC) and Mental Health Composite (MHC) scores [19]. The BDI is a validated 21-item questionnaire assessing the probability of depression, with scores ranging from 0 to 63; a score of ≥ 21 is highly suggestive of clinical depression [20]. The Guralnik short physical performance battery consists of three tests that assess patients’ physical function (sit-to-stand time, 6-min walk distance and grip strength), with scores ranging from 0 to 12 [21].

Statistical analysis

Baseline characteristics of the study population were expressed as mean (\pm SD), median [with interquartile range (IQR)] or the proportion of patients in designated subgroups (%). Analysis of variance, Kruskal–Wallis tests and chi-square tests, as appropriate, were used to compare baseline characteristics of participants with unpaid caregivers with those who reported having no unpaid caregivers.

For patients with complete Cousineau questionnaire data, potential correlates with baseline total Cousineau score were tested using linear regression and expressed as odds ratios with 95% confidence intervals. Variables significant at the $P < 0.1$ level in univariate analyses were included as factors in a multivariable model, along with the prespecified factors of age, sex, education level and number of medications per day. A P -value of < 0.1 was chosen for the hypothesis-generating univariate analyses only in order to improve statistical power.

We then tested the association between the Cousineau score and each of the following: overall score on the SF-36, PHC and MHC scores and BDI score. Each model was adjusted for the variables described above. For multivariable models, missing values were multiply imputed while incorporating auxiliary variables reflecting factors for baseline dropout, to better accommodate the assumption that missing data would be associated with the other variables used for imputation. Missing values for education level were assigned a value of ‘unknown’. Standard errors for the multivariable models were corrected for the multiple imputation.

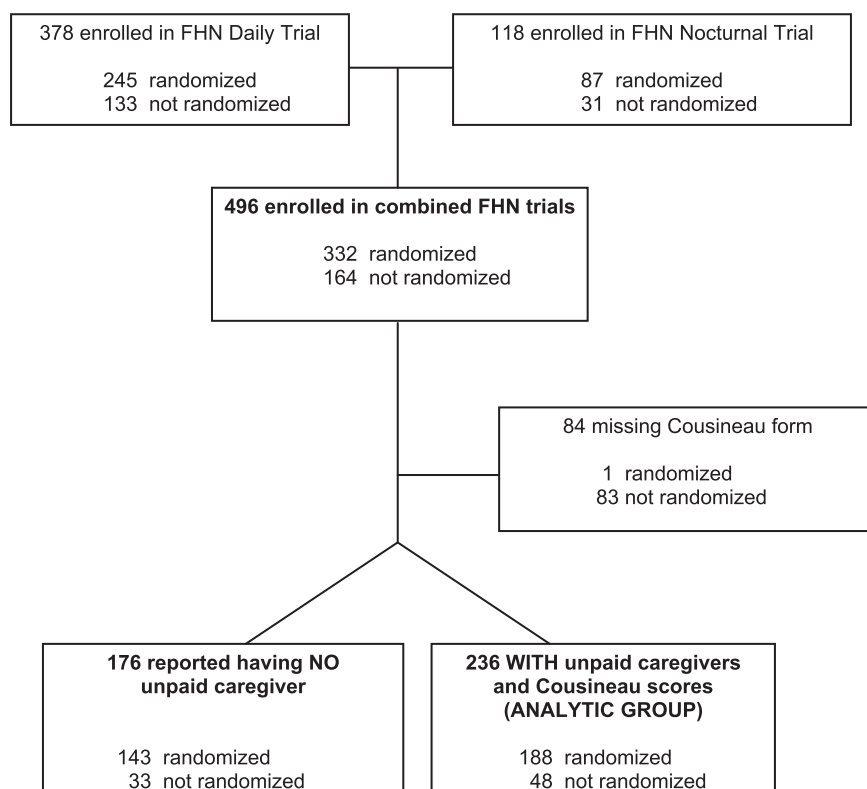


Fig. 1. Flow diagram of study subjects included in analysis of perceived caregiver burden.

Table 1. Comparison of subjects with and without unpaid caregivers^a

Variable	N = 236 with unpaid caregivers	N = 176 with no unpaid caregivers	P-value
Age (years)	51.7 ± 13.0	50.5 ± 14.5	0.42
Female	96 (41%)	64 (36%)	0.37
Black race versus other	83 (35%)	74 (42%)	0.15
Years of end-stage renal disease	0.72/2.22/6.03	1.20/3.15/6.24	0.11
Charlson comorbidity index			
0	71 (32%)	82 (50%)	<0.01
1	44 (20%)	27 (17%)	
2	43 (19%)	21 (13%)	
≥3	64 (28%)	33 (20%)	
Number of medications/day	13 ± 24	19 ± 97	0.44
SF-36 MHC	35/45/52	39/49/56	0.002
SF-36 PHC	27/33/42	33/41/48	<0.0001
Beck Depression Index	16 ± 11	12 ± 9	<0.0001
Physical performance battery	8.1 ± 2.9	8.8 ± 2.4	0.014

^aResults presented as mean ± SD, 0.25/median/0.75 or counts.

Finally, linear trends in patient characteristics corresponding to a single-question response indicating increasing levels of confidence that participants' unpaid caregivers could care for them were tested using the Jonckheere–Terpstra test and the Cochran–Armitage trend tests, as appropriate.

Two-tailed P-values of <0.05 were considered statistically significant unless otherwise specified. All analyses were conducted using SAS v9.2 (Cary, NC).

Results

Flow of study participants

The flow of study participants is graphically displayed in Figure 1. In total, 496 participants were enrolled in the two

FHN trials (378 daily trials and 118 nocturnal trials). Of these, 83 were excluded because they did not complete the Cousineau questionnaire and did not indicate whether or not they had an unpaid caregiver. One additional subject was excluded as the Cousineau questionnaire was incompletely answered. There were no significant differences in baseline characteristics (including age, sex, race, years on dialysis and Charlson comorbidity index) among participants with missing versus participants with complete Cousineau data.

Of the remaining 412 participants, 176 indicated that they had no unpaid caregiver. There were thus 236 participants with unpaid caregivers and Cousineau scores who

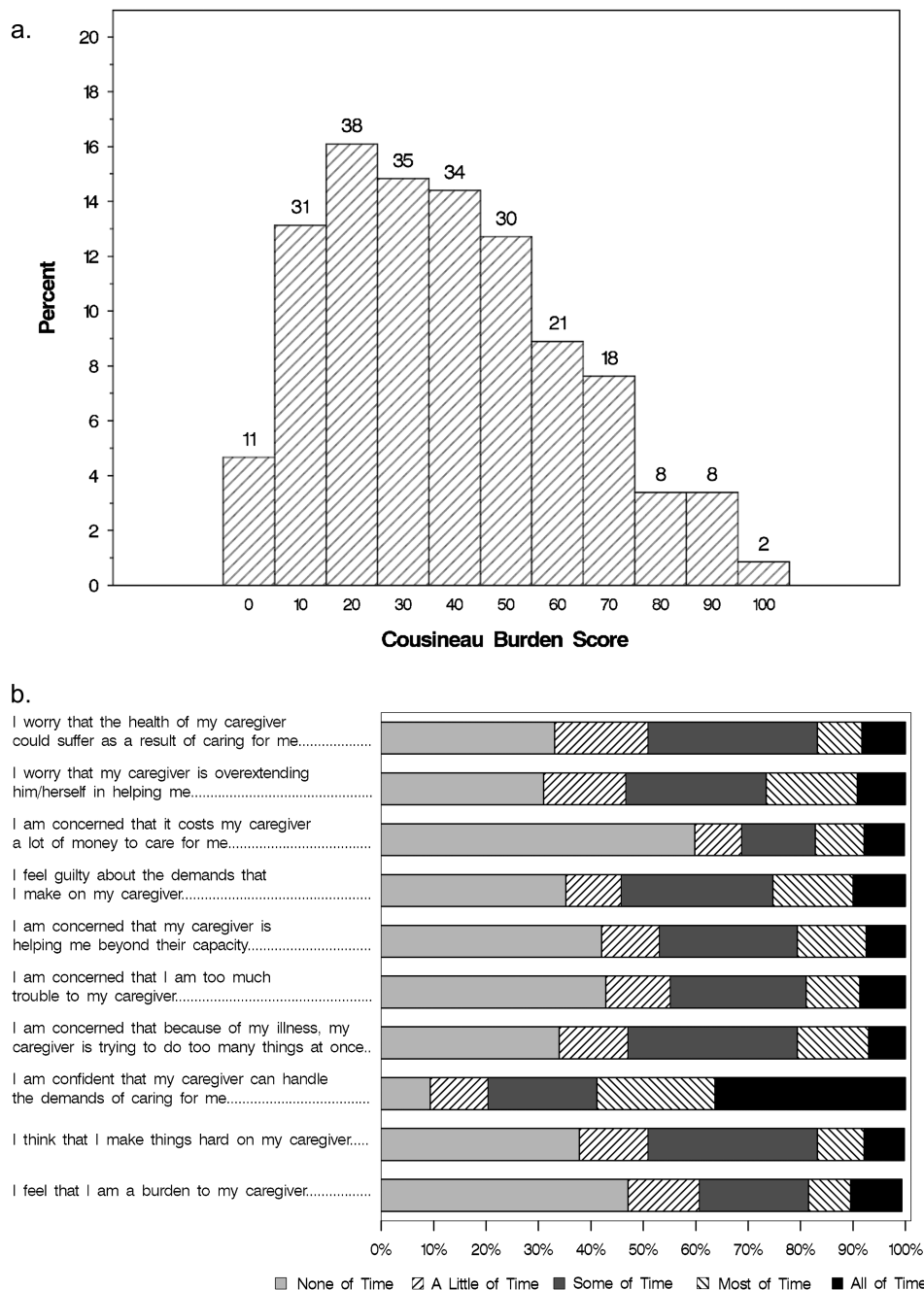


Fig. 2. (a) Histogram of total Cousineau questionnaire scores. (b) Stacked column graphs of scores on individual items in Cousineau questionnaire.

were included in the analytic group. Compared to the 176 participants without unpaid caregivers, those with unpaid caregivers had significantly higher Charlson comorbidity scores, lower overall SF-36 PHC and MHC scores, lower short physical performance battery scores and higher BDI scores (Table 1).

Distribution of and factors associated with Cousineau scores

The median score in the 236 participants who completed the Cousineau questionnaire was 35 of 100, but there was a wide

range of scores (IQR 20–53). Distributions of total score and scores for each item are presented in Figure 2a and b.

Age, sex, race, years of end-stage renal disease, education level, comorbidity and travel time to the dialysis unit were unrelated to the extent of perceived burden. Associations between perceived burden with number of medications per day (direct association), and with ability to be randomized (inverse association), were of borderline significance ($0.05 < P < 0.10$) (Table 2). However, higher perceived burden was significantly associated with lower SF-36 PHC scores, lower SF-36 MHC scores and higher BDI scores (Table 2).

Table 2. Factors associated with perceived burden (unadjusted, univariate models)^a

Variable	N	Linear regression coefficients (95% CI)	P-value
Age (years)	236	-0.17 (-0.40 to 0.055)	0.14
Female	236	3.55 (-2.52 to 9.63)	0.25
Black race versus other	236	-3.25 (-9.46 to 2.96)	0.31
ESRD vintage (years)	236	-0.09 (-0.58 to 0.40)	0.72
Education: high school graduate versus > high school	224	-0.86 (-9.08 to 7.36)	0.84
Education: high school graduate versus ≤ high school		2.18 (-5.16 to 9.52)	0.56
US resident versus Canadian	236	1.92 (-6.05 to 9.89)	0.64
Randomized versus did not complete baseline period	236	-6.85 (-14.2 to 0.53)	0.069
Travel time to dialysis unit (round trip, per 10 min)	236	0.085 (-0.53 to 0.70)	0.79
Charlson comorbidity index	222	0.56 (-1.08 to 2.21)	0.50
Number of medications/day	236	0.11 (-0.012 to 0.24)	0.077
MHC (SF-36)	235	-0.85 (-1.08 to -0.62)	<0.0001
PHC (SF-36)	235	-0.98 (-1.26 to -0.70)	<0.0001
Short physical performance battery score (0 worst to 12 best)	212	-0.43 (-1.50 to 0.64)	0.43
Beck Depression Index (overall score)	235	0.99 (0.70 to 1.28)	<0.0001

^aCI, confidence interval.**Table 3.** Factors associated with perceived burden (adjusted, multivariable models, N = 236)^a

Variable	Linear regression coefficients (95% CI)	P-value
Initial multivariable model ^b		
Age (years)	-0.17 (0.40 to 0.05)	0.13
Female	3.9 (-2.2 to 10.0)	0.20
High school or less versus ≥high school	1.9 (-4.3 to 8.0)	0.55
Number of medications/day	0.12 (0.004 to 0.3)	0.058
Randomized (versus did not complete baseline period)	-4.4 (-12.5 to 3.7)	0.29
Additional multivariable models evaluating quality of life and depression		
SF-36 MHC ^c	-0.81 (-0.11 to 0.57)	<0.0001
SF-36 PHC ^c	-0.94 (-1.23 to -0.65)	<0.0001
Beck Depression Index ^c (overall score)	0.80 (0.54 to 1.06)	<0.0001

MHC = Mental Health Composite, PHC = Physical Health Composite.

^aCI, confidence interval.^bAge and sex were specified for inclusion in the multivariable model a priori, while education level, medications and randomization status were included based on P < 0.10 in univariate models.^cEach variable tested separately, while controlling for age, sex, education level, number of medications/day and physical function score.

In multivariable models, randomization status was not statistically significant but the trend toward a direct association between number of medications per day and perceived burden remained (data not shown). In addition, the associations among scores on the PHC, MHC and BDI with perceived burden all remained statistically significant with multivariable adjustment (Table 3).

Discussion

In this large diverse cohort of patients on maintenance HD in North America, nearly two-thirds reported having an unpaid caregiver. Unlike several other studies, we did not objectively define 'caregiver'. This approach removed any preconceived notions about what a caregiver should be or does, allowing us to more accurately examine participants' perceptions. We found that participants with unpaid caregivers appeared to have more comorbidity, worse quality

of life, more depression and to be lower functioning than those who reported having no unpaid caregiver. These findings suggest that participants interpreted having an unpaid caregiver primarily if they perceived that another person was helping them with their daily living and medical needs. Conversely, those who felt they were more independent were more likely to report having no unpaid caregiver.

While the majority of participants reported having unpaid caregivers, the total perceived burden score was widely distributed with more than one-quarter of participants having extremely high perceptions of burden. We found no associations among perceived caregiver burden with demographic factors, including age, sex, race and level of education. We were surprised that the Charlson score as well as individual comorbid conditions were not significantly associated with perceived caregiver burden. Perceived burden also did not affect the ability of patients to be randomized. As hypothesized, however, we found that perceived caregiver burden was directly associated with depression (as measured by

BDI) and inversely associated with self-reported physical and mental health (as measured by SF-36). Although one cannot attribute causality in a cross-sectional study, our study leads us to hypothesize whether strategies aimed to reduce the perceived burden on caregivers might lead to improvements in depression and HRQoL in patients on HD.

Our study results extend the findings of Cousineau *et al.* [18] to a younger more racially diverse cohort. Cousineau *et al.* originally developed and validated their 10-item questionnaire in 100 Canadian patients on maintenance HD. In that study, there were also significant associations among perceived burden and self-reported physical and mental health [18].

Scrutiny of the individual questions on the Cousineau questionnaire suggests that financial burden was less distressing to most participants, being reported as a concern at least some of the time in fewer than one-third of the participants, while more than half worried that their caregivers were overextended and/or doing too many things at once. Approximately the same number felt guilty about the demands they made on their caregivers. It is intriguing, however, that when participants were asked questions in the context of themselves, i.e. whether they were 'too much trouble' or 'a burden', rather than in the context of their caregivers, fewer than half responded as being concerned at least some of the time. This discrepancy suggests that some individuals recognize their caregivers as being burdened generally, with the subject him or herself being only partly responsible. It is also interesting that a majority of participants were reassured that their caregivers could cope with the burden most or all of the time. We had hypothesized that participants who perceived that their caregivers could cope with the burden would have less depression and better HRQoL than their counterparts, but this contention was not supported by our study results.

This study has several strengths. The sample size was relatively large and participants were recruited from dialysis programs throughout the USA and Canada. Detailed clinical data and validated metrics of HRQoL, depression and multiple functional domains were simultaneously assessed. We used a number of analytic techniques, including multivariable regression and multiple imputation to reduce confounding factors and bias. The study also has several important limitations. Most importantly, the study sample was not fully representative of the HD population in North America. To be included in the study, participants had to be willing to consider an intensive dialytic intervention, or in the case of participants enrolled in the nocturnal study, participants additionally were willing and able to perform HD at home. That being said, aside from being younger and having longer than average duration of end-stage renal disease, the FHN Trials participants were similar in demographic, clinical and laboratory characteristics to the broad population of patients on HD. In the event that FHN study participants were healthier and/or more motivated than non-participants, the perceived burden on caregivers may have been underestimated. The study participants were from North America, so these results may not be fully generalizable to patients and their families from other regions, such as Europe, the far East and Latin America, where >50% of the world's patients on dialysis reside.

Nevertheless, patients on dialysis all over the world have unpaid caregivers; while there may be important cultural differences related to patient and caregiver burden, these data will be informative to patients, families and providers worldwide. Due to logistical constraints of the trial, we were unable to query caregivers about their perceived burden, unlike several prior studies. Evaluating caregivers, family, friends, community members and dialysis care providers would allow a more comprehensive global view of the burden of caring for patients with end-stage renal disease.

Conclusions

In summary, we conducted a cross-sectional analysis of participants enrolled in the FHN clinical trials and determined a high degree of perceived caregiver burden among patients receiving HD. The extent of perceived caregiver burden was unrelated to demographic factors and comorbidity but was significantly associated with poorer self-reported HRQoL and depression. The FHN trials will provide us with a unique opportunity to evaluate how frequent HD influences perceived caregiver burden as well as the relationships among perceived caregiver burden, HRQoL, physical and mental health and depression. Such an evaluation will be important in helping to establish the net benefits/detriments of these intensive dialytic strategies.

Conflict of interest statement. None declared.

(See related article by Rutkowski *et al.* Daily hemodialysis and caregivers burden. *Nephrol Dial Transplant* 2011; 26: 2074–2076.)

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Peritoneal macrophage infiltration is correlated with baseline peritoneal solute transport rate in peritoneal dialysis patients

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Abstract

Background. High baseline peritoneal solute transport rate is reportedly associated with reduced patient and technique survival in continuous peritoneal dialysis (PD) patients. However, the determinants of baseline peritoneal solute transport rate remain uncertain. The aim of this study was to investigate the relationship between peritoneal local inflammation, angiogenesis and systemic inflammation and baseline peritoneal permeability.

Methods. Peritoneal biopsy specimens from 42 pre-dialysis uraemic patients and 11 control individuals were investigated. Immunohistochemistry for CD68-positive macrophages, chymase- and tryptase-positive mast cells, interleukin-6 (IL-6)-positive cells, CD3-positive T cells, CD20-positive B cells, neutrophils and CD31- and pathologic anatomie Leiden-endothelium (PAL-E)-positive blood vessels in the peritoneum was performed. Baseline dialysate-to-plasma ratio for creatinine (D/P Cr)

was determined within 6 months of PD induction. Clinical and laboratory parameters were measured at the time of peritoneal biopsy. Factors associated with peritoneal permeability were assessed by multiple linear regression analysis.

Results. Pre-dialysis uraemic peritoneum showed infiltration by CD68-positive macrophages, and mast cells, as compared with controls. Baseline D/P Cr was correlated with density of CD68-positive macrophages ($P < 0.001$), IL-6-positive cells ($P < 0.001$), CD31-positive ($P < 0.05$) and PAL-E-positive blood vessels ($P < 0.05$) and serum albumin ($P < 0.05$). However, baseline peritoneal permeability was not correlated with infiltration by mast cells, B cells, T cells, neutrophils, serum C-reactive protein or other clinical factors. On multiple linear regression analysis, the number of CD68-positive macrophages in peritoneum was an independent predictor for baseline peritoneal permeability ($P = 0.009$).